Abstract

The present invention provides methods for producing exogenous and chimeric antibodies in avians. One aspect of the present invention is a method of producing avians or avian cells lacking endogenous immunoglobulin light chain and heavy chain loci, or portions

5   thereof, and having at least a portion of at least one exogenous immunoglobulin locus. The present invention provides a method for obtaining an avian cell with a deletion in an endogenous immunoglobulin locus by by introducing a targeting construct comprising two regions of sequences which are homologous to the 5' and 3' flanking sequences of the region to be deleted in the wild-type locus. In addition, the invention provides methods for inserting exogenous

10   immunoglobulin gene loci into the genome of an avian cell. A second aspect of the invention is the generation of transgenic avian species or transgenic avian cells for producing chimeric antibodies. The avian host is characterized by: (1) being incapable of producing endogenous immunoglobulin; and (2) having at least a portion of an exogenous immunoglobulin locus comprising at least one immunoglobulin constant region or portion thereof. Specific binding

15   proteins with xenogenic regions can be produced in a viable avian host by immunization of the avian host with an appropriate immunogen. Another aspect of the invention is the isolation of antibody-producing cells from a transgenic avian of the present invention that has been immunized with an antigen of interest. The cells can be immortalized for the production of antibody in culture. The immortalized cells can be used for the isolation of cDNAs encoding

20   immunoglobulin heavy and light chains or portions thereof. The cDNAs can be reintroduced to cell lines, including mammalian cell lines for efficient production of monoclonal antibodies. The cDNAs can optionally be mutated or altered, for example, such that they encode higher avidity antibodies or chimeric immunoglobulin molecules, prior to reintroduction into cell lines.

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IMG-00112.P.1
Singh